

**MARKED VERSION OF PAGE ONE OF THE SPECIFICATION**

**PAIN TREATMENT BY PERIPHERAL ADMINISTRATION OF A NEUROTOXIN**

by

Kei Roger Aoki, Minglei Cui and Stephen Jenkins

**CROSS REFERENCE**

This application is a continuation of application serial number 10/199,222, filed July 18, 2002, which is a continuation of serial number 09/550,371, filed April 14, 2000, now U.S. patent 6,464,986 B1, the entire contents of which prior application and patent are incorporated herein by reference in their entireties.

**BACKGROUND**

The present invention relates to methods for treating pain. In particular, the present invention relates to methods for treating pain by peripheral administration of a neurotoxin.

Many, if not most ailments of the body cause pain. Generally pain is experienced when the free nerve endings which constitute the pain receptors in the skin as well as in certain internal tissues are subjected to mechanical, thermal, chemical or other noxious stimuli. The pain receptors can transmit signals along afferent neurons into the central nervous system and thence to the brain.

The causes of pain can include inflammation, injury, disease, muscle spasm and the onset of a neuropathic event or syndrome. Ineffectively treated pain can be devastating to the person experiencing it by limiting function, reducing mobility, complicating sleep, and dramatically interfering with the quality of life.

A muscle spasm can lead to stimulation of mechanosensitive pain receptors thereby causing a sensation of pain. Thus, pain can arise from or be due to a

muscle spasm. Additionally, the spasm can indirectly stimulate the pain receptors by compressing onto blood vessels, causing ischemia in the tissue, which in turn releases pain inducing substances that stimulate pain receptors to cause pain sensations. Furthermore, a muscle spasm can cause a localized pH reduction which can be perceived as or which can engender pain signals. Hence, pain can be a secondary effect of a muscle spasm or muscle hypertonicity.